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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/780,205	02/09/2001	Stanislaus Laurens Johan Wouters	4753US	7934

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TRASK BRITT
P.O. BOX 2550
SALT LAKE CITY, UT 84110

EXAMINER	
BELYAVSKYI, MICHAIL A	
ART UNIT	**PAPER NUMBER**
1644	

DATE MAILED: 01/30/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/780,205	WOUTERS ET AL.	
	Examiner	Art Unit	
	Michail A Belyavskyi	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 October 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-2, 6, 9-11, 13-31, 33-37 and 40- 43* is/are pending in the application.

4a) Of the above claim(s) *23,25 and 26* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,6,9-11,13-22,24,27-31,33-37 and 40-43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/22/2003 has been entered.

Claims 1-2, 6, 9-11, 13-31, 33-37 and 40- 43 are pending

Claims 23 and 25-26 stand withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b) as being drawn to a nonelected invention.

Claims 1-2, 6, 9-11, 13-22, 24, 27-31, 33-37 and 40- 43 are under consideration in the instant application.

In view of the amendment, filed 10/22/2003 the following rejections remain

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:
The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 1-2, 6, 9-11, 13-22, 24, 27-31, 33-37 and 40- 43 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an antibody or fragment thereof and composition comprising said antibody or fragments which binds to an epitope and broken from an epitope under specifically chosen conditions recited in Table 1 does not reasonably provide enablement for an antibody or fragment thereof which binds to en epitope and broken from an epitope under broadly recited conditions for the same reasons set forth in the previous Office Action, mailed 04/22/03.

Applicant's arguments, filed 10/22/2003 have been fully considered, but have not been found convincing.

Applicant asserts that: (i) since the specification disclosed working examples of antibody which binds to an epitope and broken from an epitope under specifically chosen conditions recited in

Table 1 , one of ordinary skill in the art would be able to make and use the claimed antibodies without undue experimentation (ii) claims were amended and now do not recite overlapping ranges.

Contrary to Applicant assertion, the issue raised by the Examiner was that Applicant has not provided sufficient guidance to enable one skill in the art to use an antibody or fragment thereof which binds to en epitope and broken from an epitope under broadly recited conditions other than under specifically chosen conditions recited in Table 1. Moreover, Applicant himself acknowledge that the specification disclosed only 16 specific clones out of the entire phage display library, which includes at the very least, millions of candidate monoclonal antibodies, possess the specific characteristics as recited in Table 1. It is the Examiner position that the specification lack of sufficient guidance and predictability in determining on how to make and use an antibody or fragments thereof that able to bind to and broken from an epitope under any broadly recited conditions, the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. In addition, Simonson et al., (US Patent 4,138,476) teach that the ability of antibody-enzymes complex to be retain in the oral cavity depends on pH and in oral fluids is vary from 5.4 to 7.8 and can be diminished by the tendency for the pH of the oral fluid to rise to the 6.2 to 7.4 range. (see entire document, column 1, lines 55-67 and column 2, lines 5-10 in particular). In addition, Weir ed. (Immunochemistry, Volume 1, 1986, p38.1-38.15 Blackwell Scientific Publication, Oxford) teaches that ability of antibody and fragment thereof to bind to and eluted from an epitope is unpredictable and varies depending on pH and ion strength (see pages 38.5-38.6 in particular).

It is also noted that the amended claim 1 and newly added claim 40 still recites overlapping ranges of pH at which an antibody or fragment thereof binds to and broken from an epitope. How can mutually exclusive endpoints be achieved at the same pH and ion strength?

4. Claims 1-2, 6, 9-11, 13-22, 24, 27-31, 33-37 and 40- 43 are rejected under 35 U.S.C. 112, first paragraph, because the specification while being enable for antibody or fragment thereof that binds to a dye and detects the plaque or binds to a diagnostically, therapeutically or cosmetically active substance and suitable for targeting and local administration of active substances for therapeutic treatment of infections in the oral cavity does not reasonable provide enablement for any antibody or fragment thereof which binds to en epitope and broken from an epitope under any broadly recited conditions for the same reasons set forth in the previous Office Action, mailed 04/22/03.

It is noted that Applicant's arguments, filed 10/22/2003 has not addressed this issue.

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-2, 6, 9-11, 13-22, 28, 30-31, 33-36 and 40-42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Beggs et al., (US Patent NO: 5,490,988) in view of Goding (Monoclonal Antibodies; Principles and Practice, 1983, Academic. Press, New York. see entire book, particularly pages 44-45) for the same reasons set forth in the previous Office Action, mailed 04/22/03.

Applicant's arguments, filed 10/22/2003 have been fully considered, but have not been found convincing.

Applicant asserts that : (i) neither Beggs et al., nor Goding teach or suggest an antibody that binds to an epitope at the first pH of between 6 and 8 or wherein the bound is broken at a second pH of between about 4 and 6 and another range of between about 8 and 8.5; (ii) Beggs et al does not even mention the disassociation of the antibody from the epitope; (iii) there is no suggestion or motivation to combine the cited references

Applicants have traversed the primary and the secondary references pointing to the differences between the claims and the disclosure in each reference. Applicant is respectfully reminded that the rejection is under 35 USC103 and that unobviousness cannot be established by attacking the references individually when the rejection is based on the combination of the references. see In re Keller, 642 F.2d 4B, 208 USPQ 871, 882 (CCPA 1981) See MPEP 2145. This applicant has not done, but rather argues the references individually and not their combination. One cannot show non-obviousness by attacking references individually where the rejections are based on a combination of references. In re Young 403 F.2d 759, 150 USPQ 725 (CCPA 1968).

In response to applicant's arguments that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See In re Fine 5 USPQ2d 1596 (Fed. Cir

1988) and In re Jones 21 USPQ2d 1941 (Fed. Cir. 1992). In this case Beggs et al, teach an antibody and antibody fragment, comprising F (ab) or Fv fragments that are able to bind to a target site through antibody –antigen binding at conditions lie within physiologically acceptable limits (see entire document , column 1, lines 39-41 and column 2, lines 18-20 in particular). pH of between 6 and 8 would be considered by one of ordinary skill in the art to lie within physiological limits. Beggs et al., further teach that antibody or antibody fragment is capable of use in a target or temporally diagnostic of externally accessible parts of a human body, particularly bind to an antigenic component of dental plaque under physiologically acceptable limits (see column 4, lines 16-30 in particular). Beggs et al., also teach that the antibody or fragment thereof binds therapeutic active agent, wherein therapeutic agent comprises an enzyme (see column 5, lines 19-42. in particular). The antibody fragment is a fragment of an antibody to *Streptococcus. mutans* and the therapeutic agent is glucose oxidase (column 4, lines 22-27 in particularly). Begges et al., also teach that the antibody or fragment thereof will be used to detect plaque in oral cavity or capable of bleaching teeth (column 4, lines 25-60 in particular). Beggs et al., also teach that antibody and the therapeutic agents are incorporated in one or more pharmaceutically acceptable dilutent or carrier (column 5, lines 44-46 in particular). Beggs et al., also teach composition useful as a teeth cleaning agent, mouthwash, toothpaste comprising antibody or fragment thereof (column 5, lines 65-67 and column 6, lines 1-6 in particular).

Goding teaches that during optimization of each purification protocol for each antibody of interest and a fragment thereof, the parameters such as pH and ionic strength play an essential role and that it is an inherent properties of all antibody and fragment to bind to an epitope under one set of specifically chosen conditions and be eluted from an epitope (bound of antibody to an epitope is broken) under specifically chosen different conditions. (pages 44-45 in particularly). It would have been obvious to one of ordinary skill in the art at the time the invention was made to determine all operable and optimal rangers of pH and ion strength at which antibody or fragment thereof binds to and eluted from an epitope, as taught by Goding and use it for antibody or fragment thereof taught by Beggs et al. Further, it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. *In re Aller*, 220 F2d 454,456,105 USPQ 233; 235 (CCPA 1955). see MPEP § 2144.05 part II A. The strongest rationale for combining reference is a recognition, expressly or implicitly in the prior art or drawn from a convincing line of reasoning based on established scientific principles or legal precedent that some advantage or expected beneficial result would have been produced by their combination In re Sernaker 17 USPQ 1, 5-6 (Fed. Cir. 1983) see MPEP 2144

6. Claims 1-2, 6, 9-11, 13-21, 24, 27, 28, 30, 31, 33-36 and 40-42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cummins et al.,(EP 0736544) in view of Goding (Monoclonal Antibodies; Principles and Practice, 1983, Academic. Press, New York. see entire book, particularly pages 44-45 for the same reasons set forth in the previous Office Action, mailed 04/22/03.

Applicant's arguments, filed 10/22/2003 have been fully considered, but have not been found convincing.

Applicant asserts that : (i) neither Cummins et al., or Cummins et al teach or suggest antibody that bound the epitope at a first pH of between about 6 and 8 or where the bound is broken at a second pH of between a range of about 4 and 6 or another range of between about 8 and 8.5; (ii) there is no suggestion or motivation to combine the cited references

Applicants have traversed the primary and the secondary references pointing to the differences between the claims and the disclosure in each reference. Applicant is respectfully reminded that the rejection is under 35 USC103 and that unobviousness cannot be established by attacking the references individually when the rejection is based on the combination of the references. see In re Keller, 642 F.2d 4B, 208 USPQ 871, 882 (CCPA 1981) See MPEP 2145. This applicant has not done, but rather argues the references individually and not their combination. One cannot show non-obviousness by attacking references individually where the rejections are based on a combination of references. In re Young 403 F.2d 759, 150 USPQ 725 (CCPA 1968).

In response to applicant's arguments that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See In re Fine 5 USPQ2d 1596 (Fed. Cir 1988) and In re Jones 21 USPQ2d 1941 (Fed. Cir. 1992). In this case , Cummins et al. teach an monoclonal antibody and fragment thereof to salivary peliicle, which are capable of recognizing cryptitopes . These antibody and fragment thereof are particularly suitable to treat oral cavity (see entire document, Abstract in particular). Cummins et al. teach various binding conditions that lie within physiologically acceptable limits, including pH and ion strength (page 4, lines 38-40 in particular). pH of between 6 and 8 would be considered by one of ordinary skill in the art to lie within physiological limits. Cummins et al. also teach that antibody and fragment thereof binds diagnostically, therapeutically or cosmetically active substance (see Abstract and pages 3-4 in particular) and can be visualized by using fluorescent labeled antibodies (page 11 in particular). Cummins et al., teach a composition comprising at least one antibody and physiologically acceptable dilutent that is useful as a cleaning agent (see Example 5 in particular) Cummins et al., teach that diagnostically, therapeutically or cosmetically active substance comprises enzyme such as a proteases, including papain, pepsin, trypsin, ficin and bromelin (page 3, lines 35-55 in particular). Cummins et al. teach the antibody or fragment thereof is capable of binding an epitope of a pathogenic micro-organism (page 3, lines 1-5 in particular) and can be used for teeth bleaching (page 3, lines 3-5 in particular).

Goding teaches that during optimization of each purification protocol for each antibody of interest and a fragment thereof, the parameters such as pH and ionic strength play an essential role and that it is an inherent properties of all antibody and fragment to bind to an epitope under one set of specifically chosen conditions and be eluted from an epitope (bound of antibody to an epitope is broken) under specifically chosen different conditions. (pages 44-45 in particularly).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to determine all operable and optimal rangers of pH and ion strength at which antibody or fragment thereof binds to and eluted from an epitope, as taught by Goding and use it for antibody or fragment thereof taught by , Cummins et al. Further, it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. *In re Aller*, 220 F2d 454,456,105 USPQ 233; 235 (CCPA 1955). see MPEP § 2144.05 part II A. The strongest rationale for combining reference is a recognition, expressly or implicitly in the prior art or drawn from a convincing line of reasoning based on established scientific principles or legal precedent that some advantage or expected beneficial result would have been produced by their combination In re Sernaker 17 USPQ 1, 5-6 (Fed. Cir. 1983) see MPEP 2144

7. Claim 29 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Beggs et al., (US Patent NO: 5,490,988) in view of Goding (Monoclonal Antibodies; Principles and Practice, 1983, Academic. Press, New York. see entire book, particularly pages 44-45) as applied to claims 1-2, 6, 9-11, 13-22, 28, 30-31, 33-36 and 40-42 as above, and further in view of Cole et al., (Immunol. &Infect. Diseases 1993, 3, 33-35) for the same reasons set forth in the previous Office Action, mailed 04/22/03.

Applicant's arguments, filed 10/22/2003 have been fully considered, but have not been found convincing.

Applicant asserts that claim 29 is non-obvious at the very least as indirectly depending from non-obvious independent claim 1.

Contrary to Applicant's assertion , as has been discussed , supra it is the Examiner position that independent Claim 1 is unpatentable over Beggs et al ., or by Cummins et al., both in view of Goding.

The teachings of Beggs et al., and Goding have been discussed, supra.

The claimed invention differs from the reference teaching only by the recitation of an antibody capable of binding *Porphyromonas gingivalis.*

Cole et al., teach an antibody to *Porphyromonas gingivalis* (see entire document, Abstract in particular) . Cole et al., further teach that this antibody play essential role in the immunopathology of periodontal disease.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to apply the teaching of Cole et al., and those of Beggs et al., and substitute antibody capable of binding to one pathogenic micro-organism associated with periodontal disease with antibody capable of binding with another pathogenic micro-organism associated with periodontal disease.

One of ordinary skill in the art at the time the invention was made would have been motivated do so, because antibody to *Porphyromonas gingivalis* are essential in the immunopathology of periodontal disease and could be used to delivery of the therapeutic agents to the target site as taught by Beggs et al.

From the combined teaching of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

8. Claims 37 and 43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Beggs et al., (US Patent NO: 5,490,988) in view of Goding (Monoclonal Antibodies; Principles and Practice, 1983, Academic. Press, New York. see entire book, particularly pages 44-45) as applied to claims 1-2, 6, 9-11, 13-22, 28, 30-31, 33-36 and 40-42 as above, and further in view of Fischer (US Patent 5,571,511)

The teachings of Beggs et al., and Goding have been discussed, supra.

The claimed invention differs from the reference teaching only by the recitation of an antibody capable of binding *Staphylovovvus epidermidis.*

US Patent '511 teach an antibody to *Staphylococcus epidermidis* (see entire document, Abstract in particular) . US Patent '511 further teach that this antibody play essential role in the new therapy for treatment of Staphylococcus infection (see column 4, lines 31-35 in particular

It would have been obvious to one of ordinary skill in the art at the time the invention was made to apply the teaching of US Patent '511 and those of Beggs et al., and substitute antibody capable of binding to one pathogenic micro-organism associated with periodontal disease with antibody capable of binding with another pathogenic micro-organism associated with periodontal disease.

One of ordinary skill in the art at the time the invention was made would have been motivated do so, because antibody to *Staphylococcus epidermidis* play essential role in the new therapy for treatment of Staphylococcus infection and could be used to delivery of the therapeutic agents to the target site as taught by Beggs et al.

From the combined teaching of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

8. No claim is allowed.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michail Belyavskyi whose telephone number is (703) 308-4232. The examiner can normally be reached Monday through Friday from 9:00 AM to 5:30 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (571) 272-0841

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Michail Belyavskyi, Ph.D.
Patent Examiner
Technology Center 1600
January 26, 2004

Phillip Gambel
PHILLIP GAMBEL, PH.D
PRIMARY EXAMINER
Tech Center 1600
1/26/04